REMARKS

This paper is being filed in response to the office action mailed October 7, 2003. The remarks below are presented to address each of the issues raised by the Examiner (in the order in which they were referred to in the office action).

Restriction Requirement

In the office action, the Examiner asserts that claims 91-94 do not read on the elected invention. Applicants respectfully disagree. Claim 91 (and claims 92-94 depending therefrom) provides for nucleic acids that encode an Apo-3 polypeptide, wherein said Apo-3 polypeptide is a *fragment* of the sequence of amino acid residues 1 to 417 of SEQ ID NO:6. As such, these nucleic acids are encompassed by the elected species. It is accordingly requested that claims 91-94 be examined along with claims 34 and 36-39.

Priority

The Examiner states in the office action that Applicant's filing date of September 23, 1996 is considered by the Office to be the priority date accorded for the instant claims. The undersigned wishes to comment on this matter of entitlement to priority as follows.

First, the Examiner has failed to provide any reasons as to why Applicant is not entitled to their earlier priority application filing date in April 1996. It is requested that the Examiner provide such reasons for the written record so that Applicant can rebut any such positions in a substantive manner.

Second, it is pointed out that if the Examiner finds Applicant is not entitled to their earlier priority application filing date, then the same standards and scrutiny must be equally applied to the priority applications of those patent references being cited by the Examiner for prior art purposes (see, e.g., Section 102(e) rejection below over Yu et al.). It is respectfully submitted that the Office cannot take inconsistent positions with respect to the question of entitlement to priority for the instant application and for art

references to be applied as prior art against the claims pending in the instant application.

Information Disclosure Statement

The Examiner has stated that the references identified as reference numbers 210-233 and 235 on Applicant's Form 1449 are improperly cited and will not be printed for publication because they lack publication dates. Applicant respectfully points out these same references (1) were cited on a similar Form 1449 in Applicant's parent application serial no. 08/828,683, (2) were accepted as being properly cited and were considered by the Examiner in the parent application, and (3) were printed on the patent issued on the parent application (see US Patent 6,469,144 issued October 22, 2002). It is believed that the Office should not take inconsistent positions on such matters and create discrepancies in the file histories of parent and divisional applications, such as these. It is requested the references be considered and an initialed copy of the Form 1449 be returned to Applicant with the next Office communication.

Specification

The specification has been amended, as shown above, to update and reflect the priority status information for the instant application.

The specification has also been amended to correct and refer to the current address of the ATCC depository.

In the office action, the Examiner noted that the Sequence Listing originally filed in the present application did not include certain sequences appearing in some figures. Applicants are filing herewith a substitute Sequence Listing (paper copy and computer-readable diskette) which is believed to be fully compliant with 37 CFR 1.821-1.825. A Certificate re Sequence Listing is also enclosed.

The substitute Sequence Listing being filed herewith provides all the sequences disclosed in the specification and figures, and certain text in the specification has been amended, as shown herein, to recite the respective SEQ ID NO:s assigned to those sequences in the

substitute Sequence Listing. Entry of the substitute Sequence Listing into the specifcation has been requested in the amendment above.

The specification (namely, the Brief Description of the Drawings on page 11) has also been amended to reflect certain numbering changes in the formal drawings which were filed in the instant application on March 22, 2002.

Section 112 Rejections

Claim 39 was rejected under Section 112, second paragraph, as being incomplete. The subject claim has been amended, as shown above, pursuant to the Examiner's suggestion. It is believed the rejection has been overcome by the amendment, and withdrawal of the rejection is requested.

Claim 34 was rejected under Section 112, first paragraph as not being adequately described in the specification. Applicant respectfully traverses this new matter rejection. Support for claim 34 can be found on at least page 65, lines 28-34 and Figure 4 of the instant application. It is expressly provided therein that a signal sequence comprises residues 1-24 of Figure 4 (SEQ ID NO:6), followed by an extracellular domain, transmembrane domain, and intracellular domain which together comprise amino acids 25-417 of Figure 4 (SEQ ID NO:6). Withdrawal of the rejection is accordingly requested.

Claims 34 and 36-39 were rejected under Section 112, first paragraph, as containing subject matter not described in the specification in a way to convey possession of the invention. Applicant respectfully traverses the rejection.

It is submitted that those skilled in the art will readily appreciate and can identify the genus of molecules encompassed by "biologically active variants". Applicant has provided in the specification a full characterization of Apo-3, both in terms of structure and function. The term "biologically active" is expressly defined in the specification (see page 19, lines 6-11) and modulation of apoptotic activity is clearly understood and

identifiable to the skilled artisan for a Apo-3 variant (also expressly defined on page 13, lines 32-35 - page 14, lines 1-14.

Section 102 Rejections

Claims 34 and 36-39 were rejected under Section 102(e) as being anticipated by Yu et al., US Patent 6,153,402. Applicant respectfully traverses this rejection for the reasons below.

The Yu et al. patent claims priority from US Provisional application no. 60/013,285 filed March 12, 1996[1] (the "first priority application") and US Provisional application no. 60/028,711 filed October 17, 1996[2] (the "second priority application"). Accordingly, the first priority application of Yu et al. was filed before the April 6, 1996 priority date of the instant application. However, the second priority application of Yu et al. was filed after the September 26, 1996 priority date of the instant application. The Yu et al. patent discloses two polypeptides, referred to as DR3-V1 and DR3 respectively, encoded by cDNA nucleic acid sequences which were cloned from a cDNA library. The first priority application of Yu et al. disclosed the sequence only of DR3-V1; the second sequence, DR3, was disclosed for the first time in the second priority application of Yu et al. filed October 17, 1996.

The first priority application of Yu et al. discloses only the cDNA sequence and deduced amino acid sequence of DR3-V1 (DDCR). This is the only actual experimental information in the specification; all of the remaining "examples" in the first priority application of Yu et al. are in fact prophetic, as can be seen from the fact that they are expressed throughout in the present tense. The function or utility of the DR3-V1 (DDCR) was solely postulated in the first priority application, based on sequence homology between the DR3-V1 (DDCR) and TNF-R. The DR3-V1 (DDCR) protein was not actually expressed or tested, and therefore its function or utility was not experimentally

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1 Cited as Reference number 26 on Applicant's Form 1449.
2 Cited as Reference number 27 on Applicant's Form 1449.

determined. It is therefore submitted that the first priority application of Yu et al. is not enabling for DR3-V1 (DDCR) and does not satisfy the requirements of Section 112 or Section 101.

The full length Apo-3 polypeptide of the instant application corresponds to the full length DR3 polypeptide of the Yu et al. patent. However, as indicated above, the DR3 polypeptide was disclosed for the first time in the Yu et al. second priority application (filed October 17, 1996), which is after the September 23, 1996 priority date of the instant application. Accordingly, the Yu et al. patent is not entitled to its March 12, 1996 priority date or its October 17, 1996 priority date for purposes of Section 102(e) against the instant claims.

A careful analysis of the disclosures of the first and second priority applications of Yu et al. clearly reveals (1) that the first application only disclosed DR3-V1 (DDCR), and disclosed DR3-V1 in a non-enabling manner and (2) that DR3 was not disclosed at all until after the priority filing dates of the instant application.

Lastly, it is pointed out that neither the Yu et al. patent nor any of its priority applications teach a sequence corresponding to the Apo-3 polypeptides presented in the instant claims.

For all these reasons, the Yu et al. patent does not have effective 102(e) prior art status against the present application and does not anticipate the present claims.

Claims 34 and 36-39 were also rejected under Section 102(e) as being anticipated by Feldmann et al., US Patent No. 5,633,145. Applicant respectfully traverses this rejection.

Applicant's claims are directed to isolated nucleic acids encoding Apo-3 polypeptides comprising amino acid residues 1 to 417, 25 to 417, 25 to 198, or 338 to 417 of SEQ ID NO:6, or a biologically active variant thereof. The Feldmann et al. patent fails to disclose any such Apo-3 polypeptides; rather the Feldmann et al. patent discloses molecules which bind to a completely different member of the TNF family, TNF-alpha. Furthermore, the Examiner is directed to the definition of "biologically active"

provided in the instant application on page 19, lines 6-11 stating expressly if refers to the ability to modulate apoptosis in at least one type of mammalian cell in vivo or ex vivo. The Feldmann et al. patent is completely silent with respect to any such apoptotic activity.

The Feldmann et al. patent therefore is not enabling for the claims presented in the instant application and cannot anticipate under Section 102(e).

For at least the reasons above, it is requested that the Section 102(e) rejections of the pending claims be withdrawn.

Date: April 7, 2004

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